

**Amendments to the Specification:**

Please amend the specification by entering the enclosed Sequence Listing.

Please amend the paragraph on page 4, lines 7-15 as follows:

Caspase 3 is a cysteine protease synthesized from a pro-enzyme by cleavage at an Asp residue to form an active protease. The active caspase 3 protease also cleaves at Asp residues. The specific recognition sequence for caspase 3 is the peptide Asp-Glu-Val-Asp (SEQ ID NO: 1). (Fernandes-Alnemri, *et al.*, *Journal of Biological Chemistry* 269:30761-30764, 1994; Nicholson, *et al.*, *Nature* 376:37-43, 1995; Srinivasula, *et al.*, *Journal of Biological Chemistry* 271:27099-27106, 1996; Schlegel, *et al.*, *Journal of Biological Chemistry* 271:1841-1844, 1996; and Casciola-Rosen, *et al.*, *J. Exp. Med.* 183:1957-1964, 1996; each of these references is hereby incorporated by reference herein.)

Please amend the paragraph on page 4, lines 28-32 as follows:

“Caspase 3 activity” refers to enzymatic activity able to cleave the caspase 3 substrate Asp-Glu-Val-Asp (“DEVD”) (SEQ ID NO: 1). Such activity is known to be produced by caspase 3 and at least one related enzyme, Mch3 $\alpha$ . (Fernandes-Alnemri, *et al.*, *Cancer Research* 55:6045-6052, 1995, which is hereby incorporated by reference herein.)

Please amend the paragraph on page 4, line 33, to page 5, line 12 as follows:

Based on the present disclosure, caspase 3 activity induced by viral infection can be measured using techniques well known in the art. Preferably, caspase 3 activity is measured using colorimetric or fluorimetric labeled substrates. More preferably, the employed substrate is DEVD (SEQ ID NO: 1) linked to a colorimetric or fluorimetric moiety. Examples of such a moiety include the colorimetric moiety *p*-nitroanilide ( $\lambda_{\text{max}} = 505 \text{ nm}$ ) and the fluorimetric moiety 7-amino-4-trifluoromethyl coumarin (“AFC”,  $\lambda_{\text{max}} = 400 \text{ nm}$ ). (Zhang, *et al.*, in *Apoptosis Detection and Assay Methods*, pages 7-14, Eds. Zhu and Chun, *BioTechniques Books*, 1998, both of which are hereby incorporated by reference herein). Colorimetric and fluorimetric labeled substrates can be employed using procedures such as those described by Zhang, *et al.*, in *Apoptosis Detection and Assay Methods*, pages 7-14, Eds. Zhu and Chun, *BioTechniques*

*Books*, 1998; and ApoAlert™ CPP32/Caspase-3 Assay Kits User Manual (PT3083-1), CLONTECH Laboratories, Inc. 1998; both of which are hereby incorporated by reference herein.

Please amend the paragraph on page 5, lines 13 to 19 as follows:

The caspase 3 assay is preferably employed on viral vaccine samples either in liquid or lyophilized form. For example, lyophilized viral samples can be reconstituted, diluted, and plated onto a cell sheet; the samples are incubated, the cells are lysed, and the cellular lysate collected and frozen at  $-70^{\circ}\text{C}$ ; after thawing on wet ice (about  $5^{\circ}\text{C}$ ) removal of cellular debris by centrifugation occurs, the supernatant is removed to a new tube containing reaction buffer, and the DEVD (SEQ ID NO: 1)-AFC substrate is incubated with the cellular supernatant.

Please amend the paragraph on page 7, lines 8 to 16 as follows:

The samples were spun in at 12,000 rpm for 5 minutes at  $4^{\circ}\text{C}$ . Supernatant (50  $\mu\text{l}$ ) was removed to a new microfuge tube and 50  $\mu\text{l}$  of 2x Reaction Buffer (Clontech: 100 mM HEPES, pH 7.4, 150 mM NaCl, 0.2% CHAPS) containing 7 mM dithiothreitol (DTT) was added. Five microliters of the 1 mM DEVD (SEQ ID NO: 1)-AFC substrate was added to the reaction and vortexed briefly. The samples were then incubated for 1 hr at  $37^{\circ}\text{C}$  in a circulating water bath. Following the incubation, 20  $\mu\text{l}$  of 10%  $\text{H}_3\text{PO}_4$  was used to quench the reaction. Quenched reactions (100  $\mu\text{l}$ ) were added to a 96 well plate and read in a TECAN fluorescent plate reader (excitation: 390 nm, emission: 480 nm, gain: 60).

Please amend the paragraph on page 9, lines 13 to 19 as follows:

A concern with using a non-purified cell lysate is the effect of non-specific substrate cleavage derived from other proteases found within the lysate. Using a specific inhibitor for caspase 3, DEVD (SEQ ID NO: 1)-CHO, the caspase 3 assay was run and analyzed. If non-specific cleavage were occurring in the assay, the addition of the inhibitor would not completely stop the substrate from being cleaved. The results shown in Table 2 indicate that adding 1 $\mu$ M DEVD (SEQ ID NO: 1)-CHO inhibitor eliminates the RFU signal.